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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/695,846	10/29/2003	Sean Philpott	454311-2220.2	7869

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EXAMINER	
HUMPHREY, LOUISE WANG ZHIYING	
ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
05/15/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/695,846	PHILPOTT ET AL.	
	Examiner	Art Unit	
	Louise Humphrey, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *20-53,60-71,76-79 and 84-110* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-32,60-63,66-69,76,77,84-86,89,93-95,98,102-104 and 107* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/10/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 20-29,33-53,64,65,70,71,78,79,87,88,90-92,96,97,99-101,105,106 and 108-110.

DETAILED ACTION

This Office Action is in response to the amendment filed 09 March 2006. Claims 1-19, 54-59, 72-75, 80-83, and 111-116 are cancelled. Claims 20-53, 60-71, 76-79, 84-110 are pending. Claims 20-29, 33-53, 64, 65, 70, 71, 78, 79, 87, 88, 90-92, 96, 97, 99-101, 105, 106, 108-110 are withdrawn. Claims 30-32, 60-63, 66-69, 76, 77, 84-86, 89, 93-95, 98, 102-104, and 107 are under final rejection.

The objection to the specification is withdrawn in response to Applicant's amendment.

Double Patenting

The nonstatutory double patenting rejection of claims 30-32, 60-63, 66-69, 76, 77, 84-86, 89, 93-95, 98, 102-104, and 107 as being unpatentable over claims 1-57 of US Patent No. 6,727,060 is maintained due to a lack of response from Applicants.

Claim Rejections - 35 U.S.C. §112

The following is a quotation of the second paragraph of 35 U.S.C. §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 30-32, 60-63, 66-69, 76, and 77 under 35 U.S.C. §112, second paragraph, as being indefinite is **withdrawn** in response to the Applicants' amendment.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 30-32, 54-57, 60-63, 66-69, 72, 73, 76, 77, 84-86, 89, 93-95, 98, 102-104, and 107 under 35 U.S.C. §103(a) as being obvious over Esté *et al.* (1999, No. AL on page 2 of IDS filed on 29 October 2003) in view of Bazan *et al.* (1998) is maintained. Applicant's arguments have been fully considered but are not persuasive.

The instant claims, as amended, are directed to a diagnostic method of determining viral tropism comprising: (a) obtaining a population of patient-derived acquired immunodeficiencv virus; (b) determining CXCR4 coreceptor use; (c) determining CCR5 coreceptor use; and (d) a determining the ratio of acquired immunodeficiency virus using the CXCR4 coreceptor compared to virus using the CCR5 coreceptor.

Examiner's rejection in the Action mailed on 17 October 2006 is summarized as follows:

Esté *et al.* disclose that bicyclam AMD3100 is a potent inhibitor of X4 HIV stains and selects for the outgrowth of R5 virus after cultivation of mixtures of the laboratory-adapted R5 (Bal) and X4 (NL4-3) HIV strains in the presence of the compound. The addition of AMD3100 to peripheral blood mononuclear cells infected with X4 or R5X4 clinical HIV isolates displaying the syncytium-inducing phenotype resulted in a complete suppression of X4 variants and a concomitant genotypic change in the V2 and V3 loops

of the envelope gp120 glycoprotein (Abstract and page 5583). Esté *et al.* further suggest that CXCR4 antagonists could be intended as deterrents for the emergence of X4 strains, more than to decrease viral load levels, which can be effectively achieved by triple drug combinations of reverse transcriptase inhibitors and protease inhibitors. The concurrent observations that they have made with both laboratory HIV strains and clinical HIV isolates point to the potential usefulness of CXCR4 antagonists in preventing the switch from R5 to X4 that is generally considered a hallmark of the onset of AIDS and/or the progression of the disease (page 5584, left column). Esté *et al.* specifically disclose a method of determination of viral fitness in a mixed virus population isolated from peripheral blood mononuclear cells (PBMC) in the presence or absence of an antiretroviral therapeutic agent, AMD3100 (pages 5578-5579). They demonstrate that, in the presence of AMD3100, only the CCR5-tropic BaL strain was detected in the proviral DNA even at the highest NL4-3/BaL ratio in the infecting virus mixture (80% CXCR4-tropic NL4-3 to 20% CCR5-tropic BaL)(Fig. 1).

Applicants argue that Esté *et al.* do not teach or suggest the diagnostic methods of the present invention as it relates to preventing the emergence of the more pathogenic strain of HIV (X4 strain) by blocking the CXCR4 coreceptor. However, this argument mischaracterizes the rejection because Esté *et al.* was offered for teaching the claimed method of determining the ratio of acquired immunodeficiency virus using the CXCR4 (X4) coreceptor compared to virus using the CCR5 (R5) coreceptor. Esté *et al.* disclose this method in Figure 1, see the legend. The HIV-1 BaL strain/isolate is the acquired immunodeficiency virus using the R5 coreceptor whereas the HIV-1 NL4-3 strain/isolate is the acquired immunodeficiency virus using the X4 coreceptor. Esté *et al.* further describe determining the coreceptor usage in each isolate by evaluation based on the sequence of the V3 region of gp120 from proviral DNA isolated from PBMC that had been infected with the virus mixtures. See page 5578, left column, the paragraph under Results. This method of determining the phenotype of the coreceptor tropism yielded results of coreceptor ratios such as 20% NL4-3 (X4 isolate) to 80% BaL

(R5 isolate) (Figure 1). Esté *et al.* further disclose determining the phenotype of the coreceptor tropism in virus cultures in the presence of AMD3100, which encompasses the limitation of after initiating the therapy in claim 32, and in the absence of AMD3100, which encompasses the limitation of before initiating the therapy in claim 31. See page 5579. Esté *et al.* hence disclose the claimed invention.

Applicants further argue that Bazan *et al.* fail to teach or suggest diagnostic methods for comparing the ratio of viral variant in a patient-derived sample using the X4 coreceptor compared to the R5 coreceptor. However, this limitation is taught by Esté *et al.*, which was applied as a primary reference (see *e.g.* page 5578). Thus, the obviousness of the combination does not hinge on whether Bazan *et al.* suggest diagnostic methods for comparing the ratio of viral variant using the X4 coreceptor compared to the R5 coreceptor. Rather, the motivation to combine the references was to use Esté reference's coreceptor determination method for evaluating patient-derived samples as taught by Bazan *et al.* Thus, the combination of Bazan *et al.* and Esté *et al.* is properly motivated.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey, Ph.D. whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9:30 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached at 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Jeffrey Parkin, Ph.D.
Primary Examiner
10 May 2007

Louise Humphrey, Ph.D.
Assistant Examiner